

Молекулярная физиология нервной системы

Лекция 3- 5(27):

Эндоканабиноиды в ретроградной
модуляции синаптической передачи

Казанский государственный
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Казань

Лекция

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Марсель, Франция

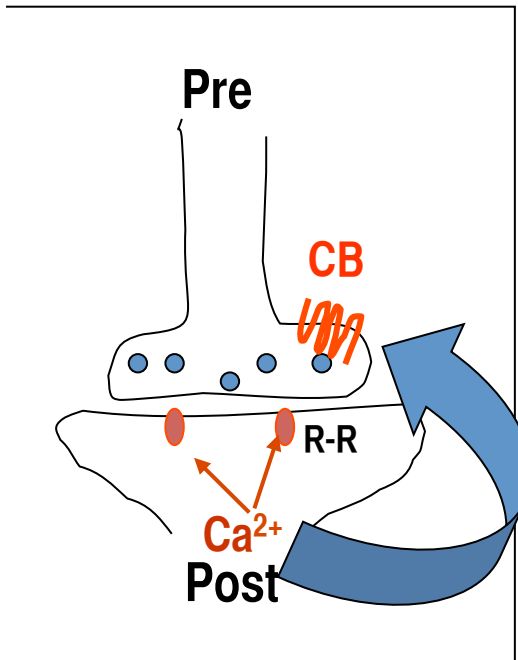
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Ретроградная сигнализация в ЦНС

Modulation of Ca^{2+} inflow

- Inactivation of Ca^{2+} channels
- Depletion of extracellular Ca^{2+}
- Action potential failure



Less transmitter in vesicles

Endocytosis:
• Modulation of recycling vesicle pools

Endosome

Ca^{2+}

CB Ca^{2+} channel

Presynaptic receptors:

- Metabotropic
- Adenosine
- Noradrenaline
- mAChR
- Cannabinoid receptors

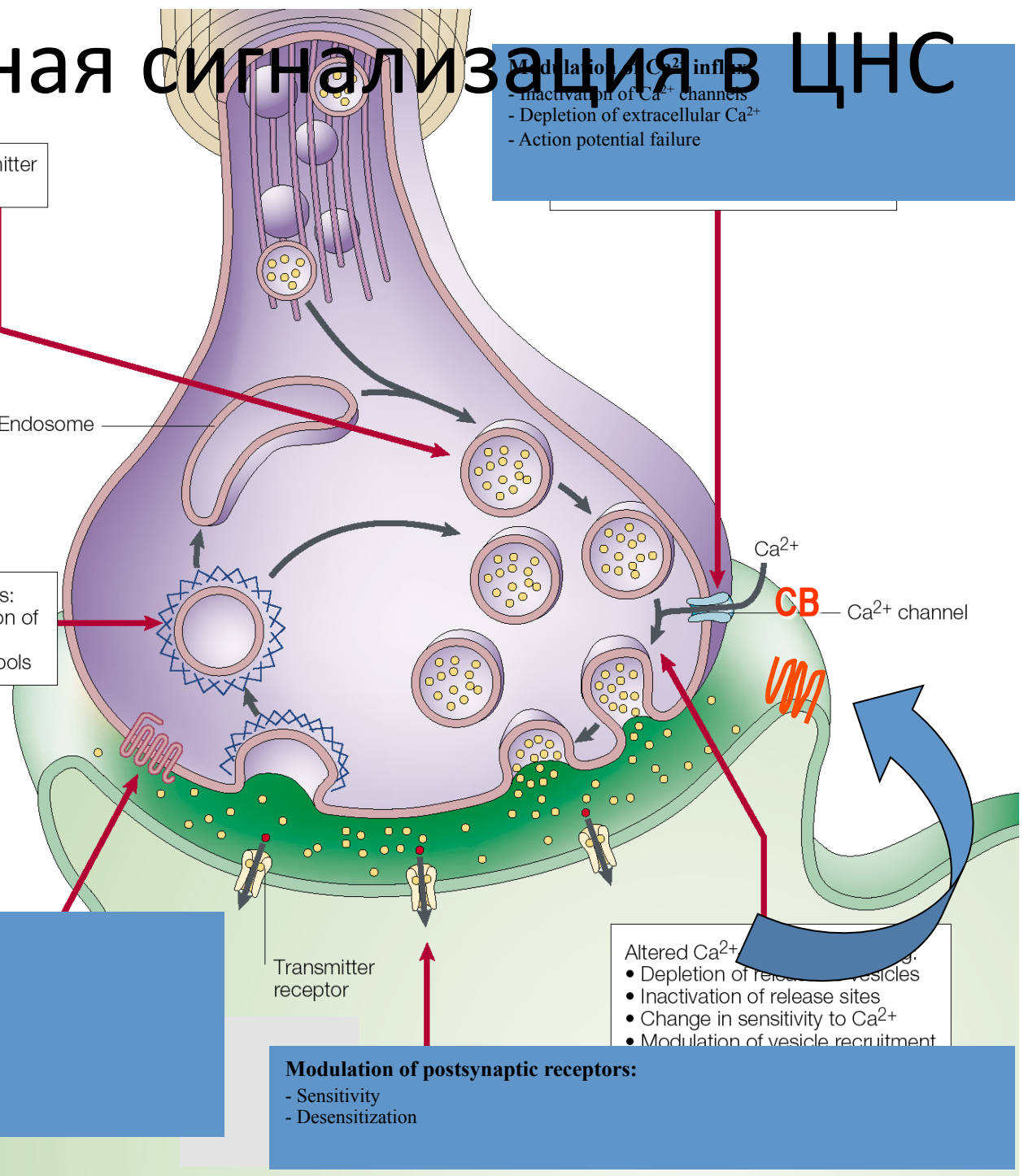
Modulation of postsynaptic receptors:

- Sensitivity
- Desensitization

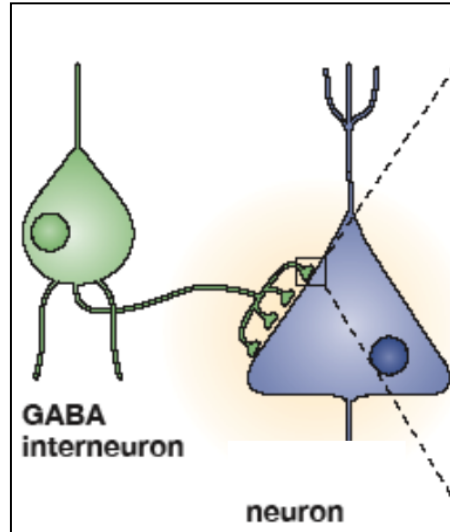
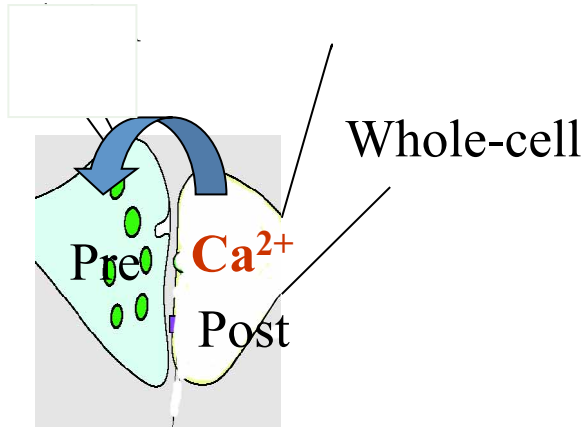
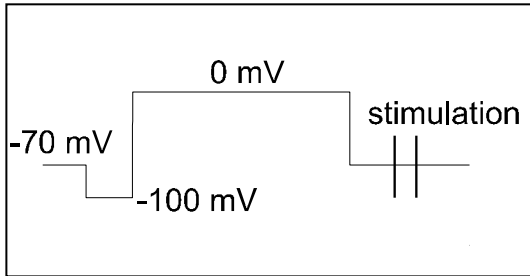
Altered Ca^{2+} inflow, e.g.

- Depletion of release sites
- Inactivation of release sites
- Change in sensitivity to Ca^{2+}
- Modulation of vesicle recruitment

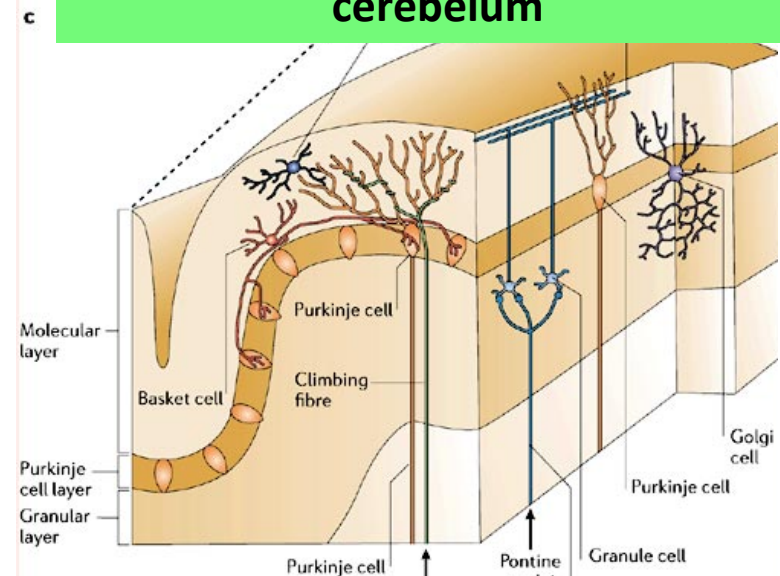
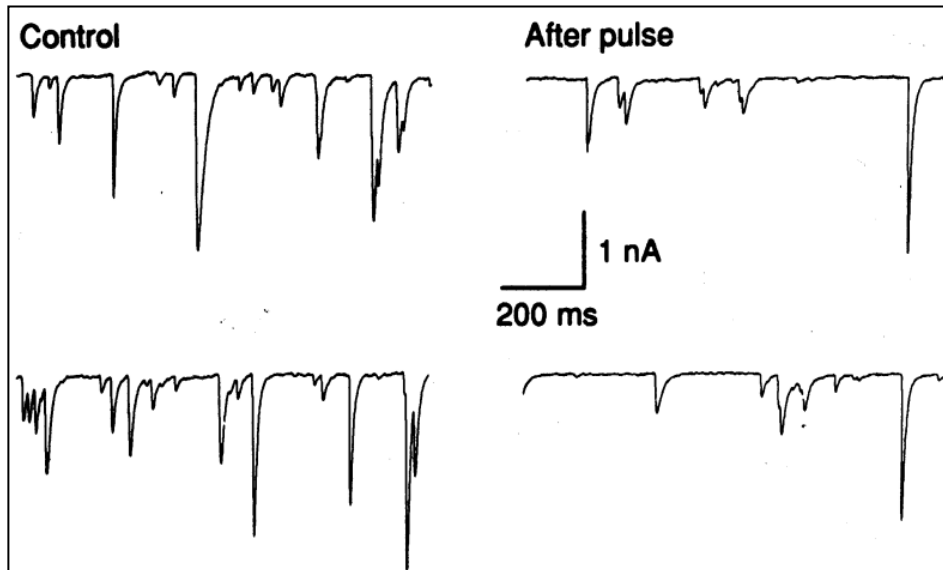
Transmitter receptor



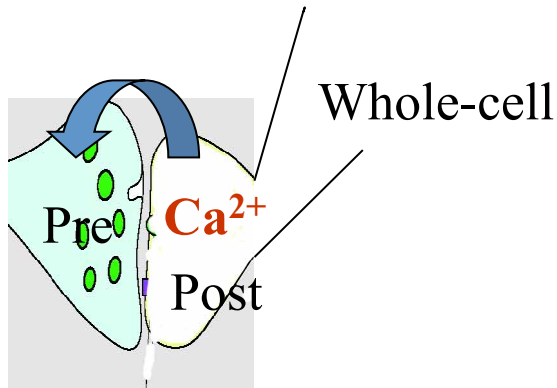
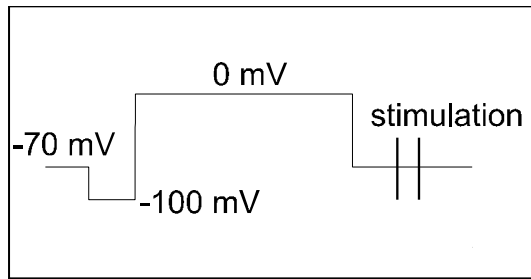
Открытие явления ретроградного торможения : DSI



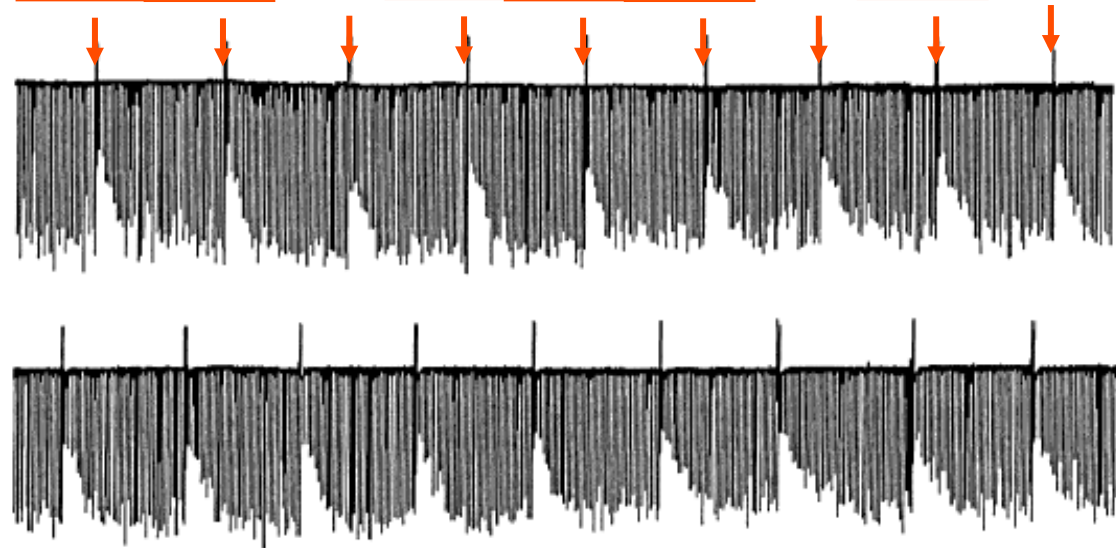
Llano, Leresche & Marty, 1991
cerebellum



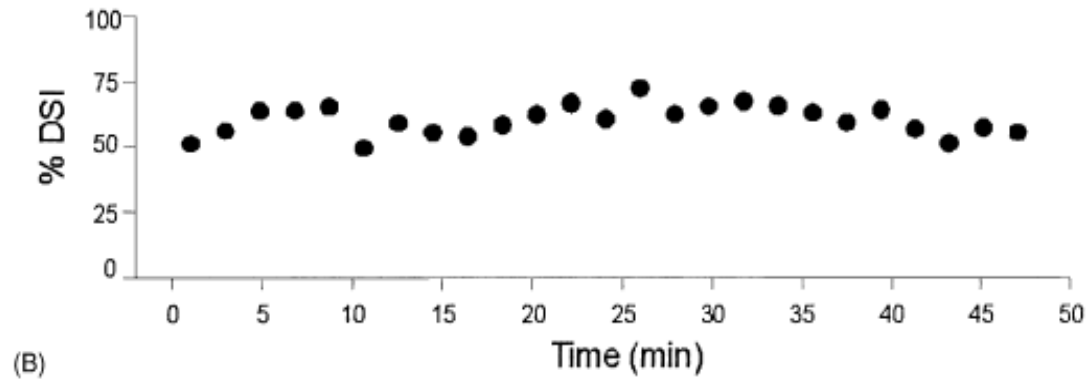
Example of hippocampal DSI



Depo Depo Depo Depo Depo Depo Depo Depo Depo

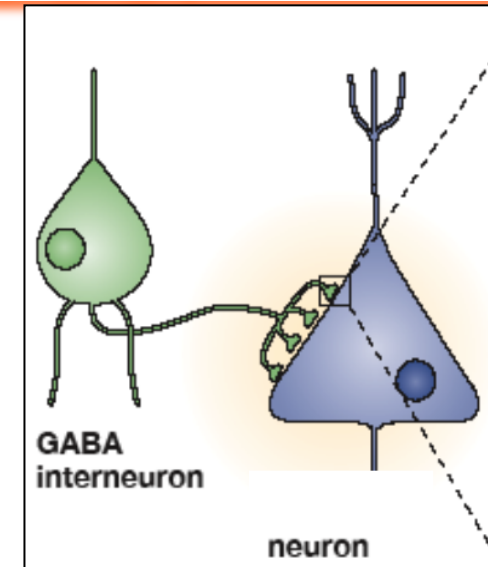
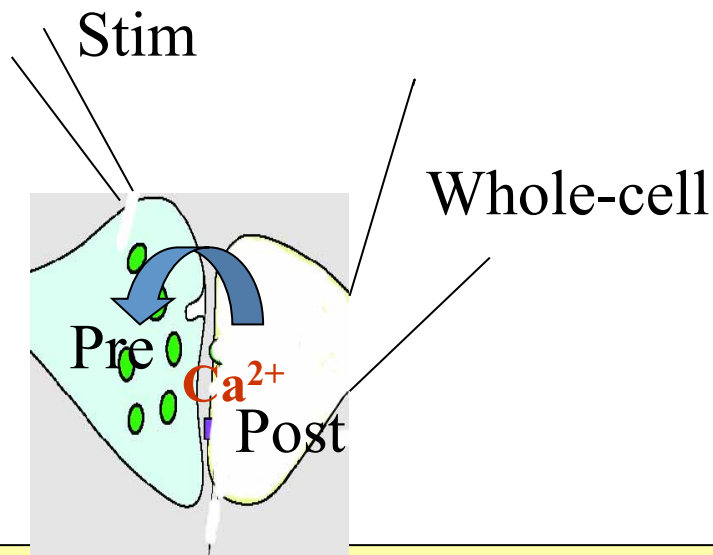


(A) 500 pA
200 s

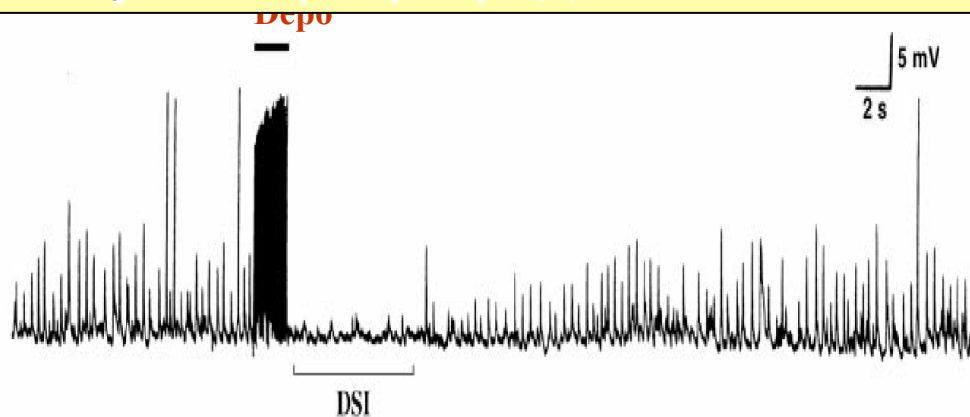


Pitler and Alger, 1992, hippocampus

Основные свойства DSI



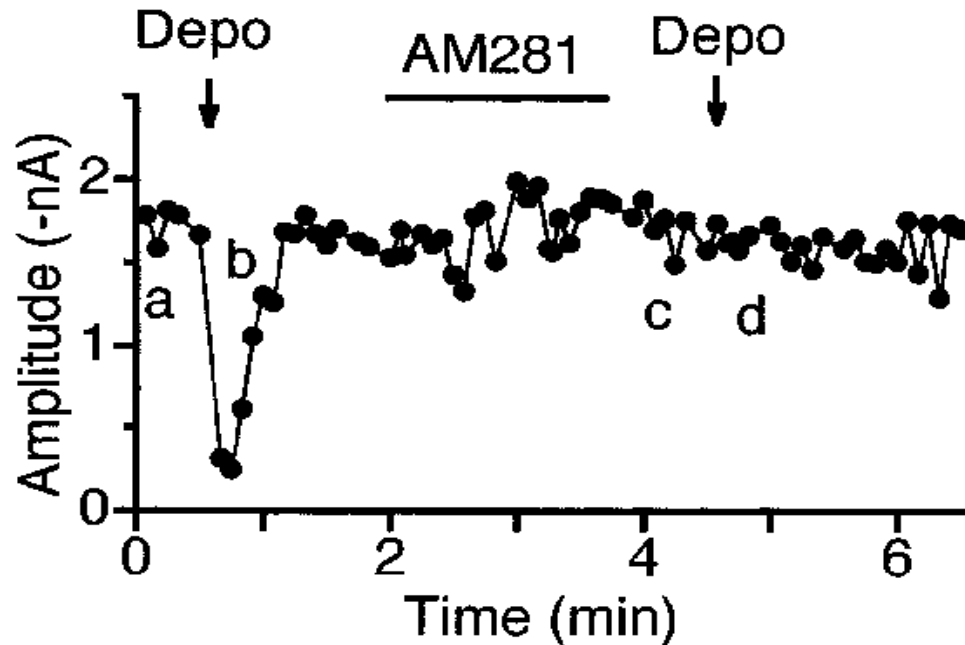
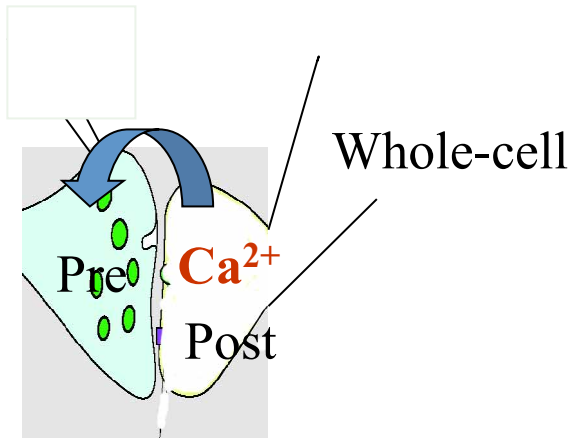
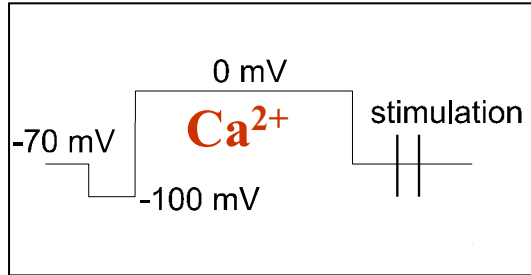
- Причина: уменьшение выброса нейромедиатора из пресинапса
- Требуется повышения Ca в постсинаптической клетке
- Результат ретроградной сигнализации



Llano et al, 1991 cerebellum

Pitler and Alger, 1992, hippocampus

Retrograde signals for DSI: endocannabinoids

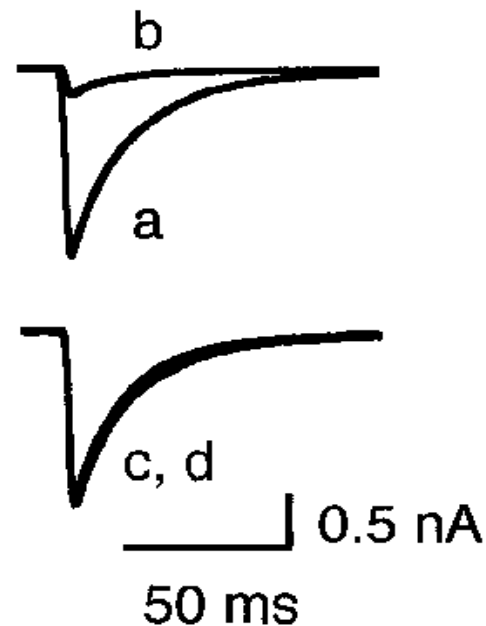


Wilson & Nicoll, 2001

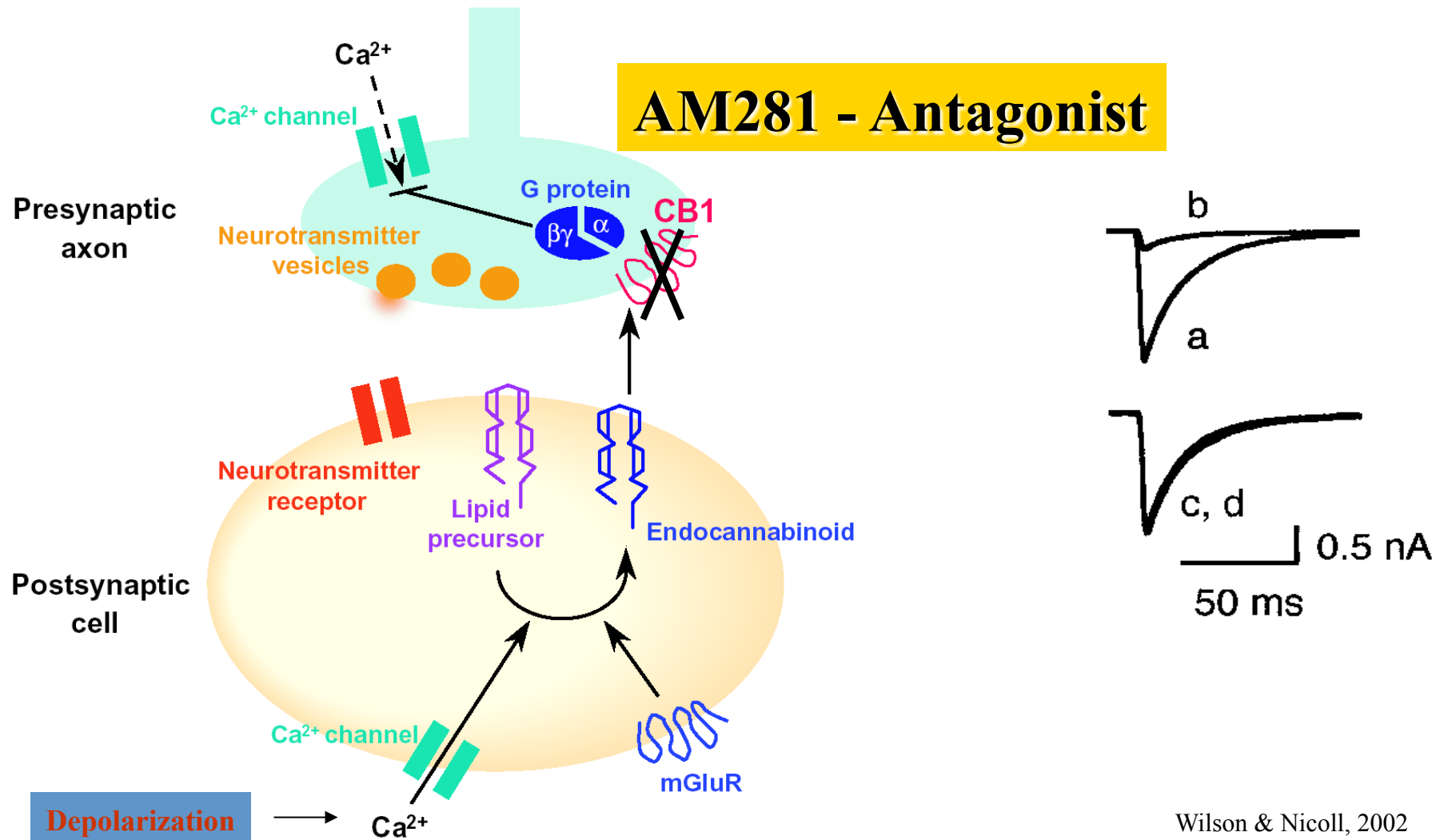
Kreitzer & Regehr, 2001

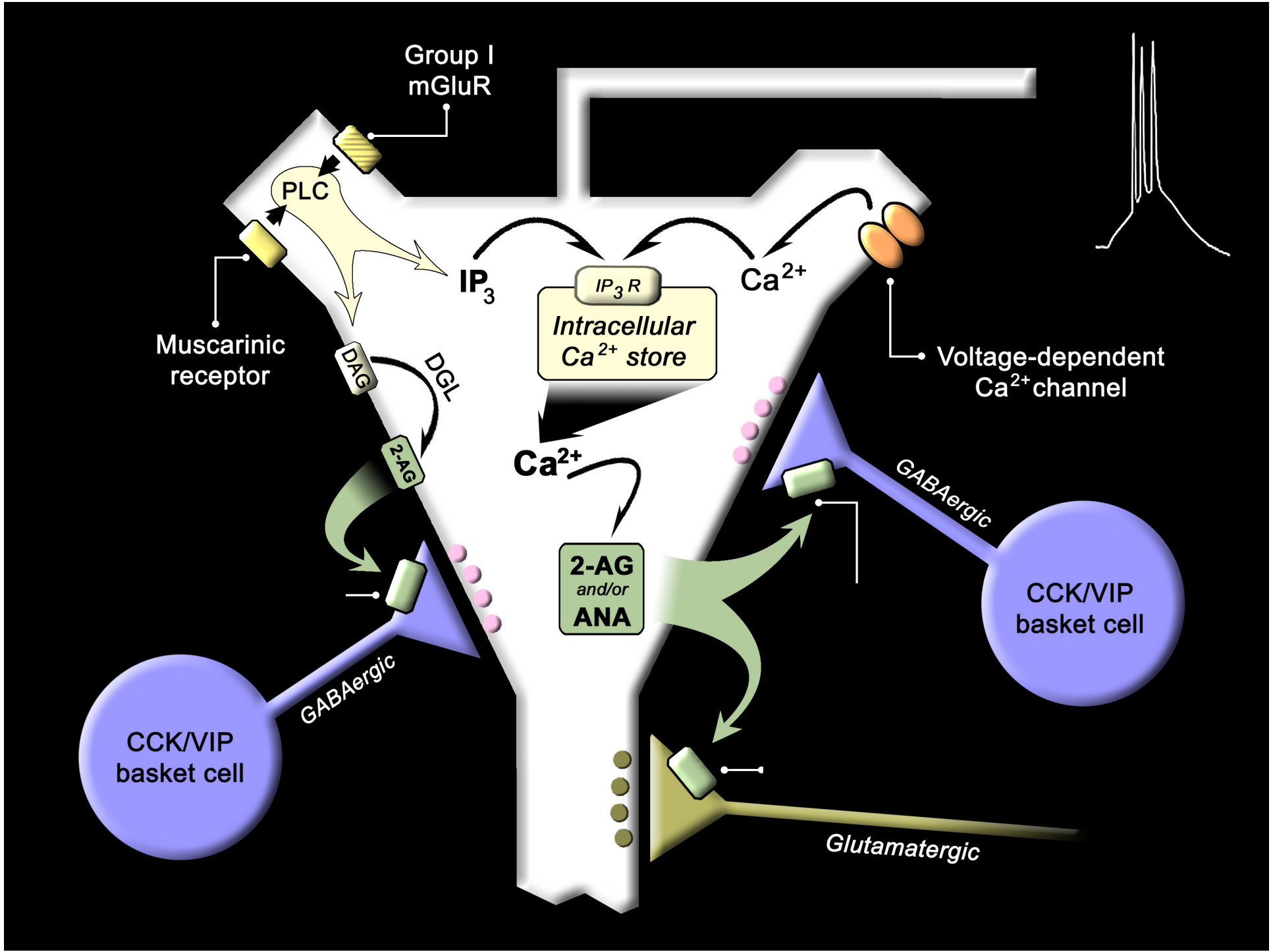
Ohno-Shosaku et al., 2001

Diana et al., 2002

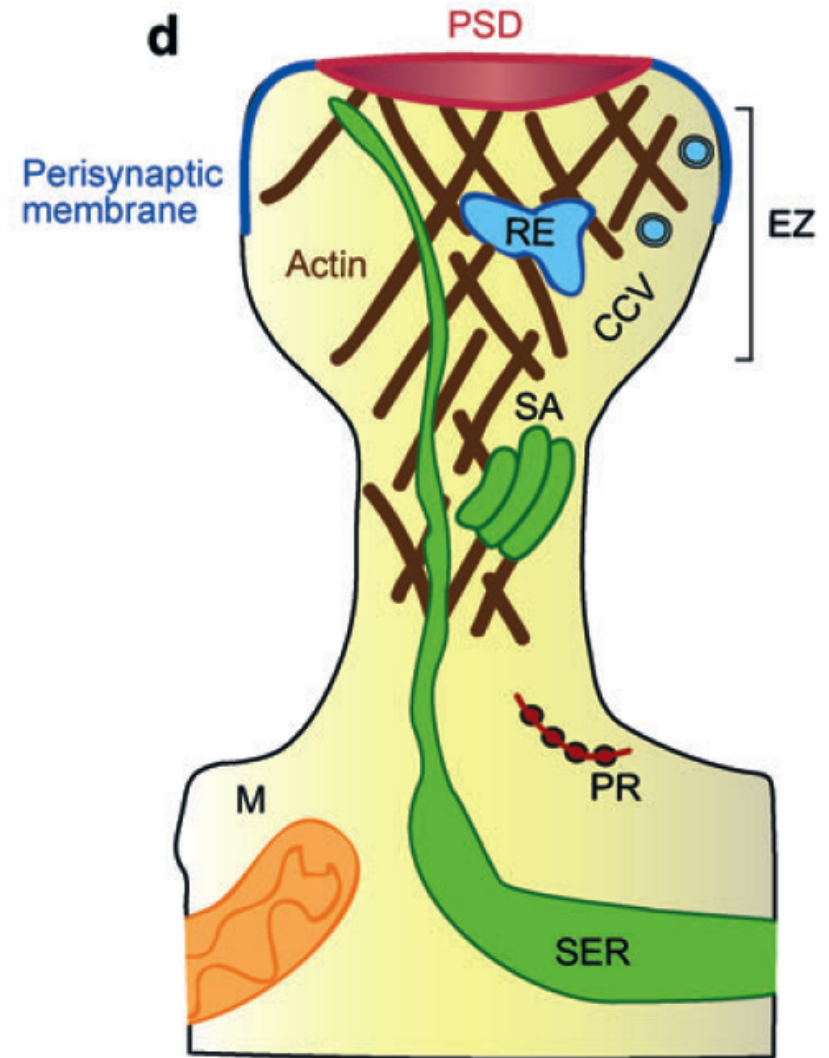
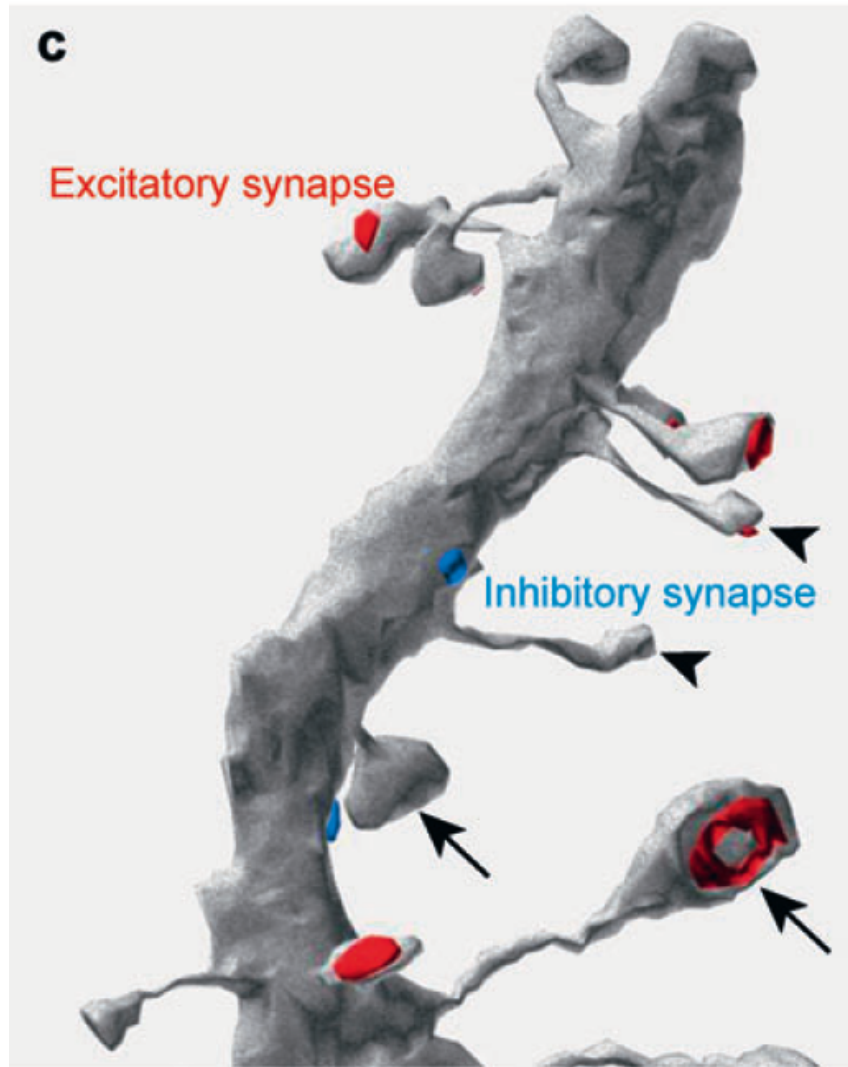


Ca²⁺-induced retrograde signaling by endocannabinoids

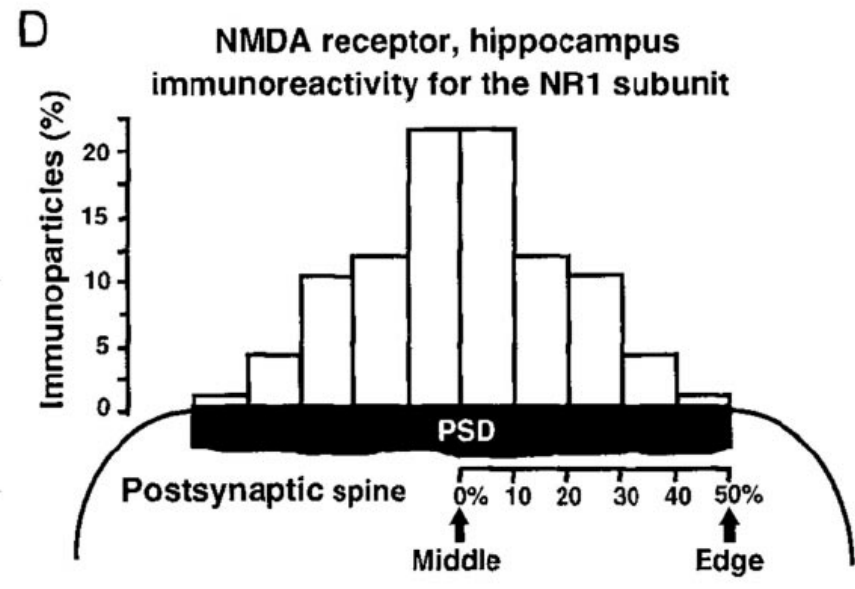
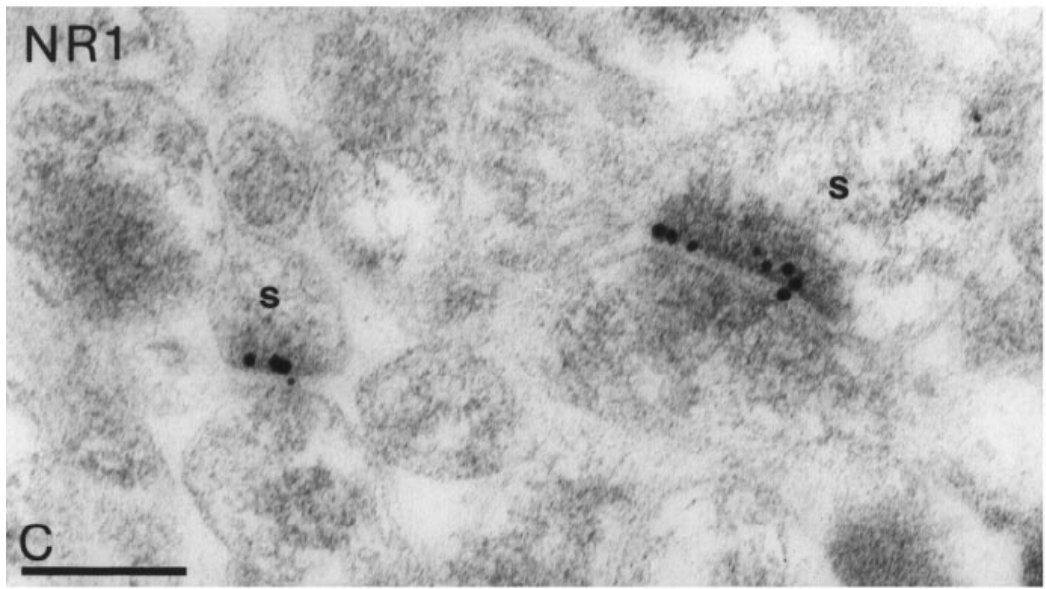
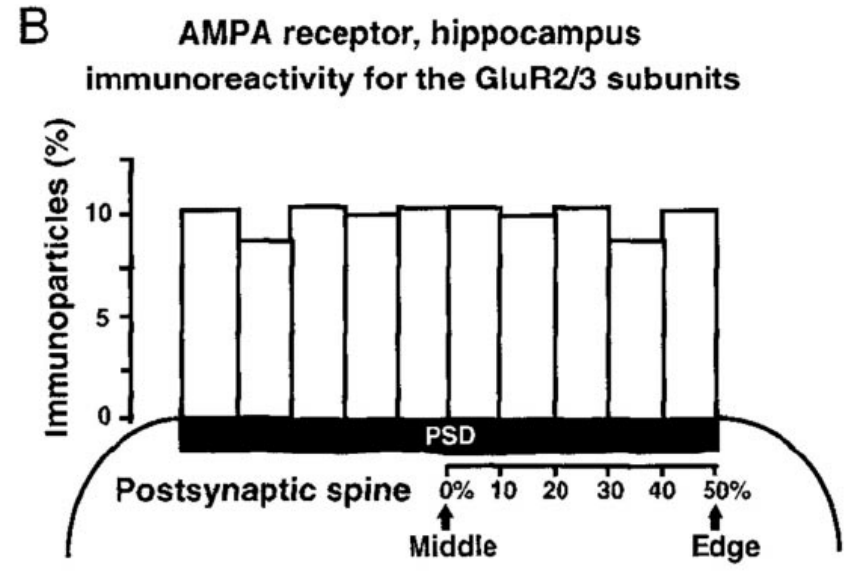
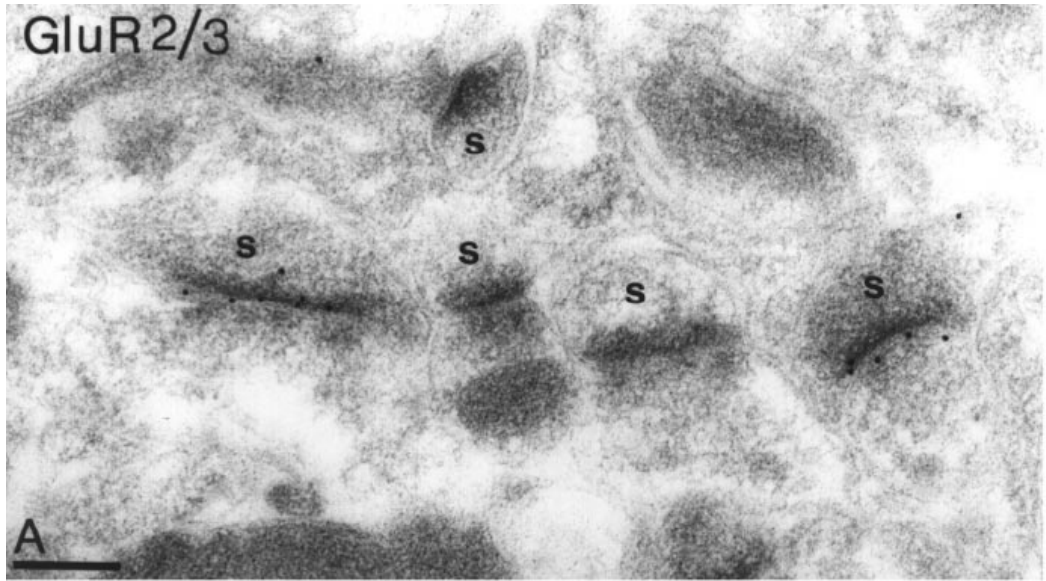




Synapses on dendrite & spine organization

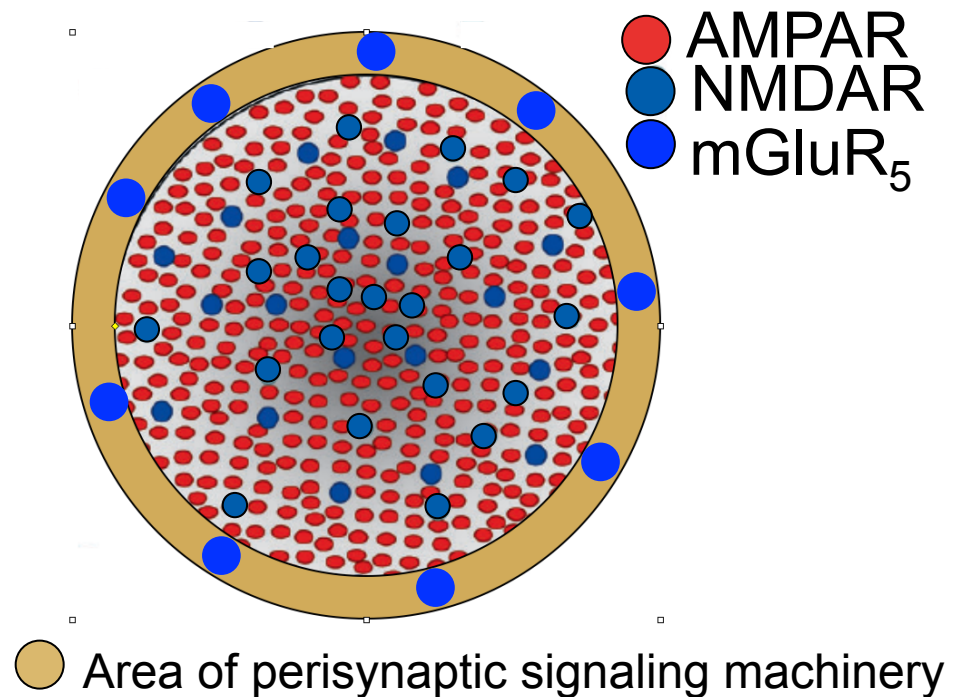
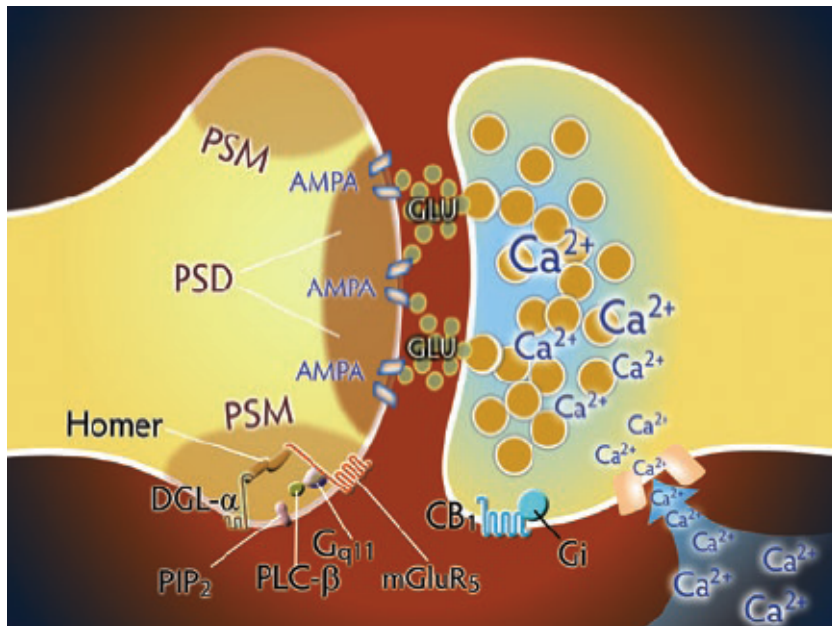
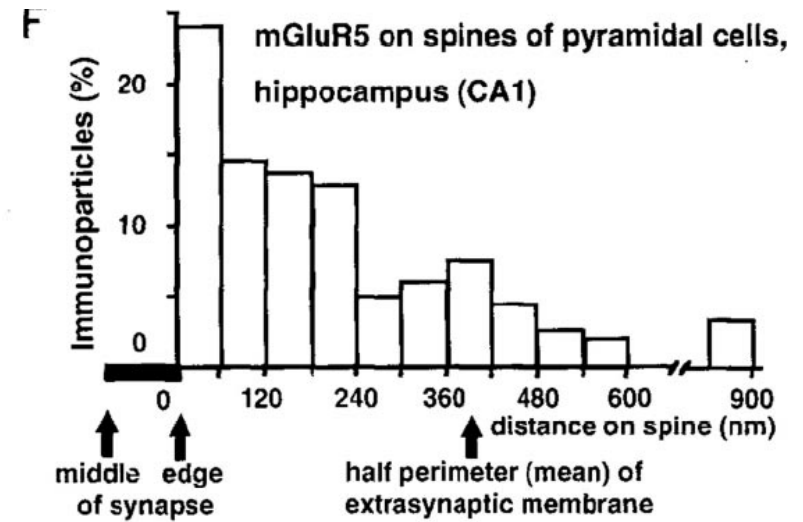
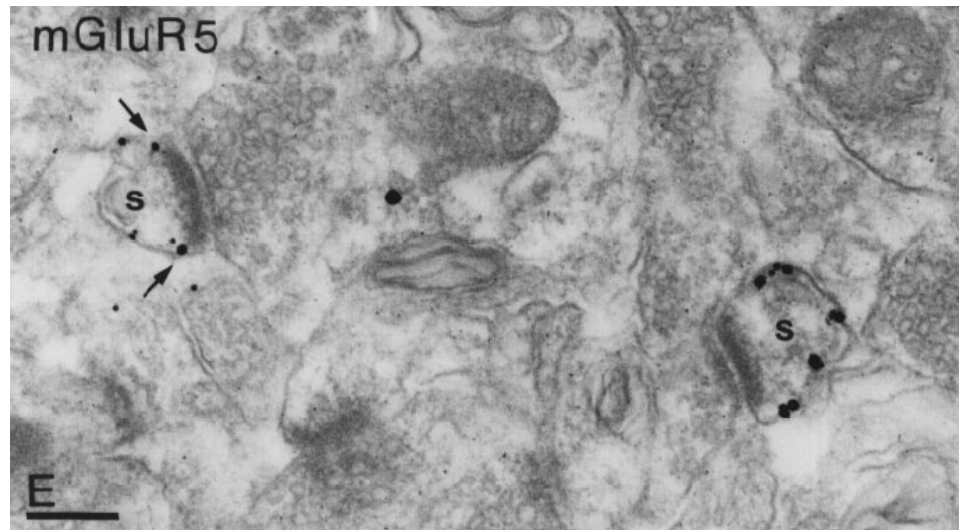


Distribution of AMPA & NMDA receptors in synapses

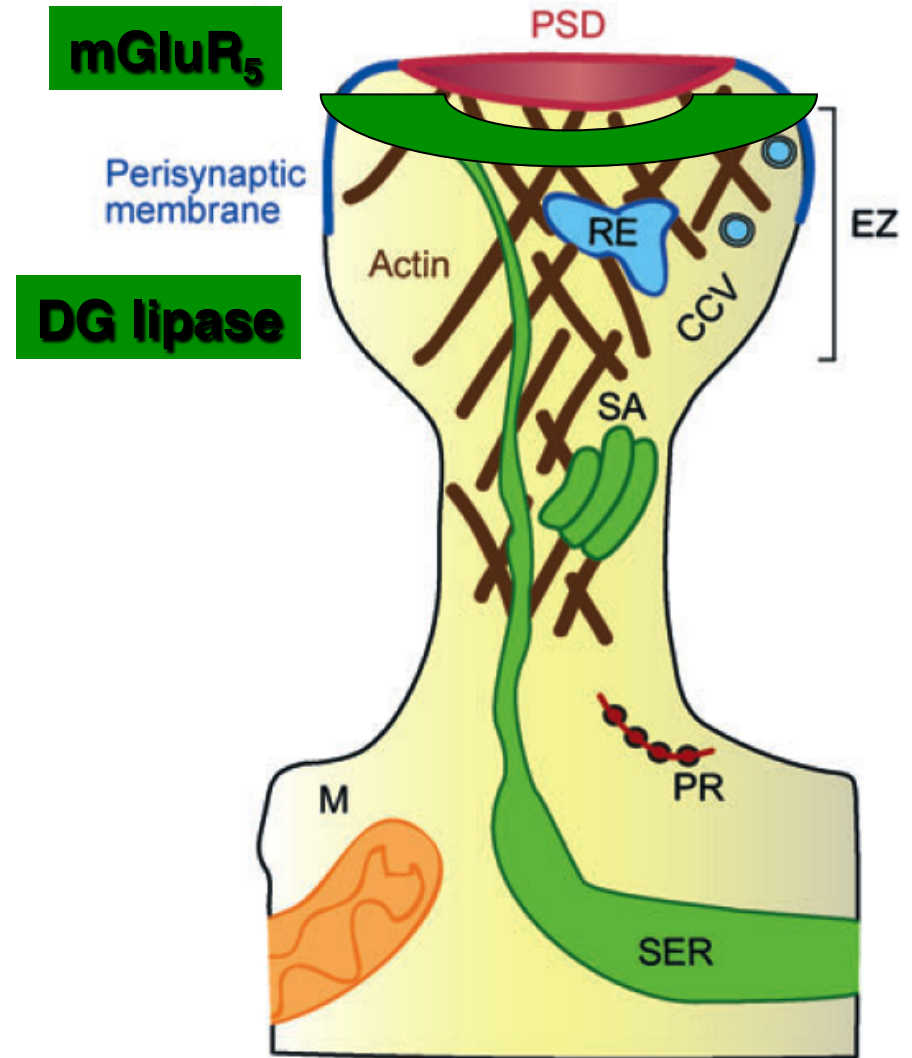
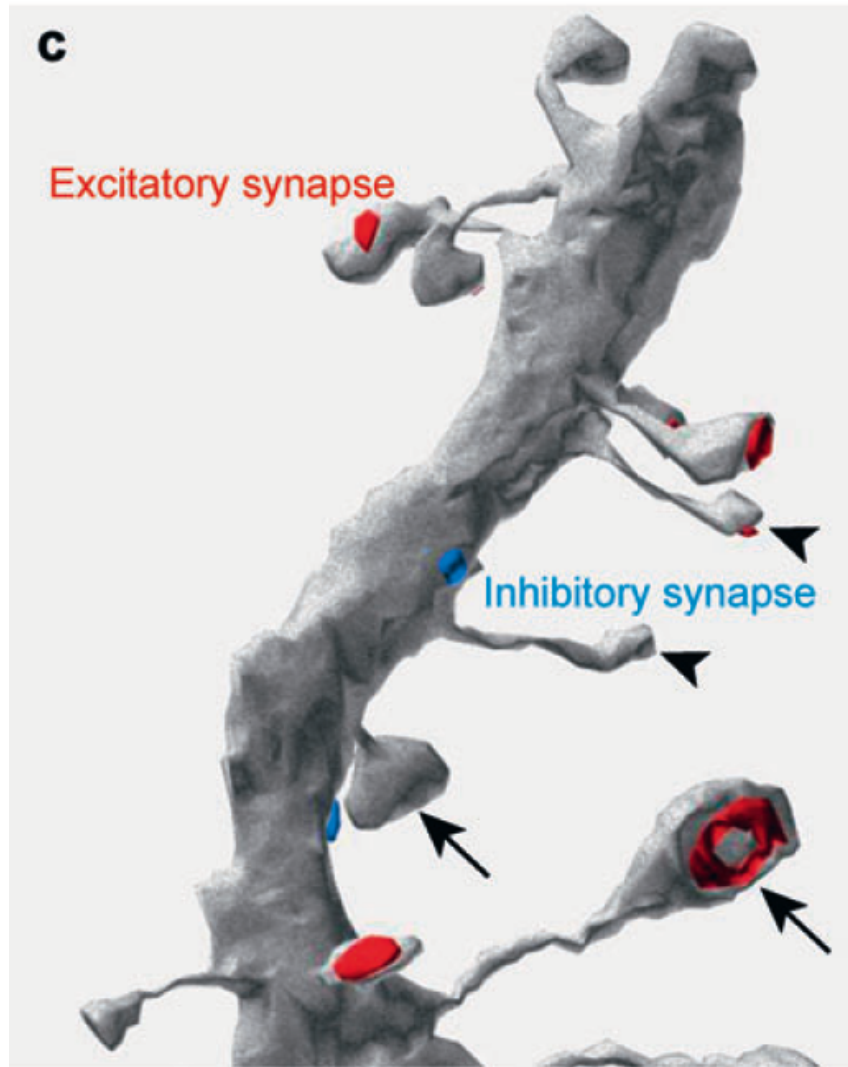


Somogyi et al., 1998

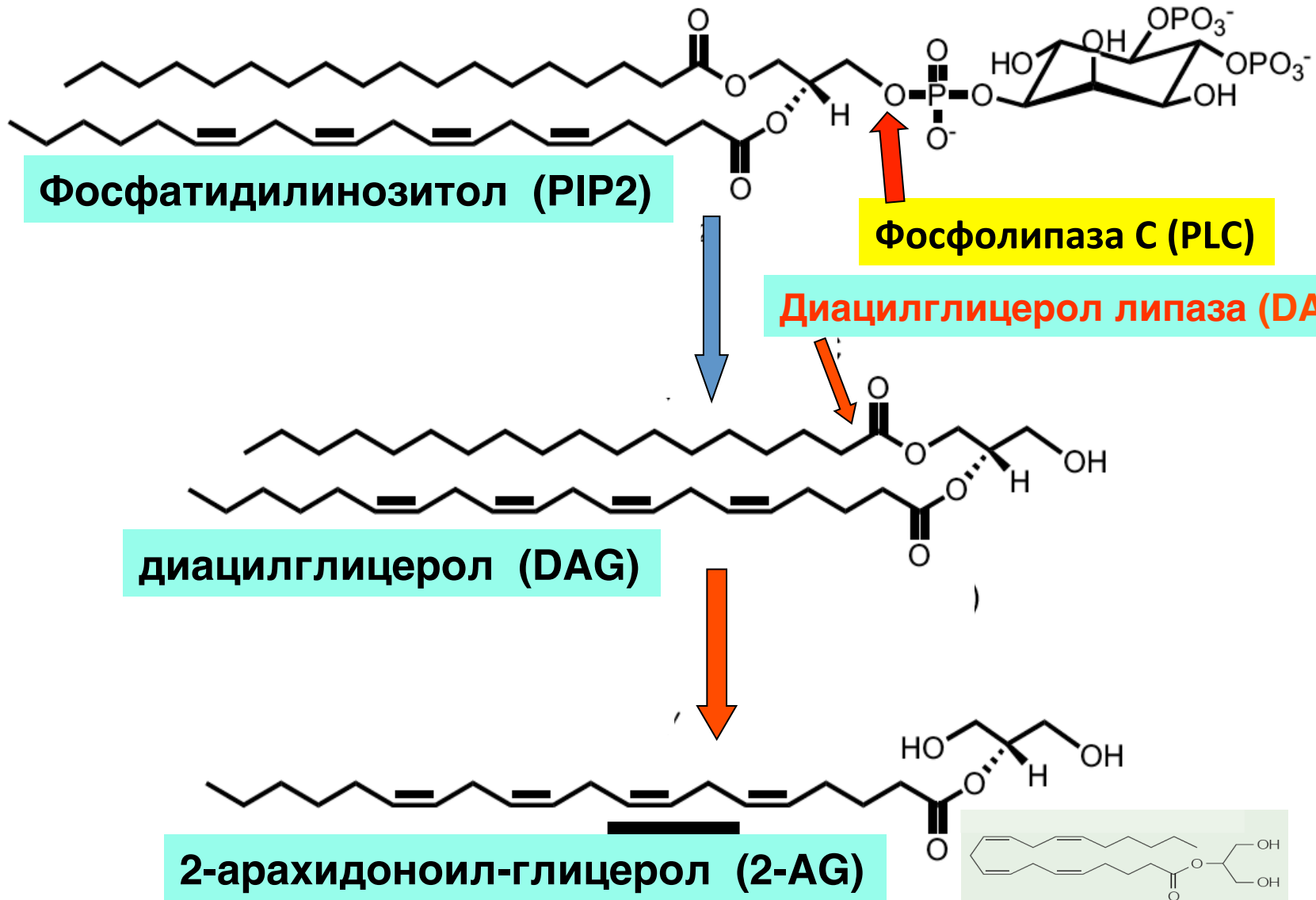
Distribution of mGlu receptors in synapses



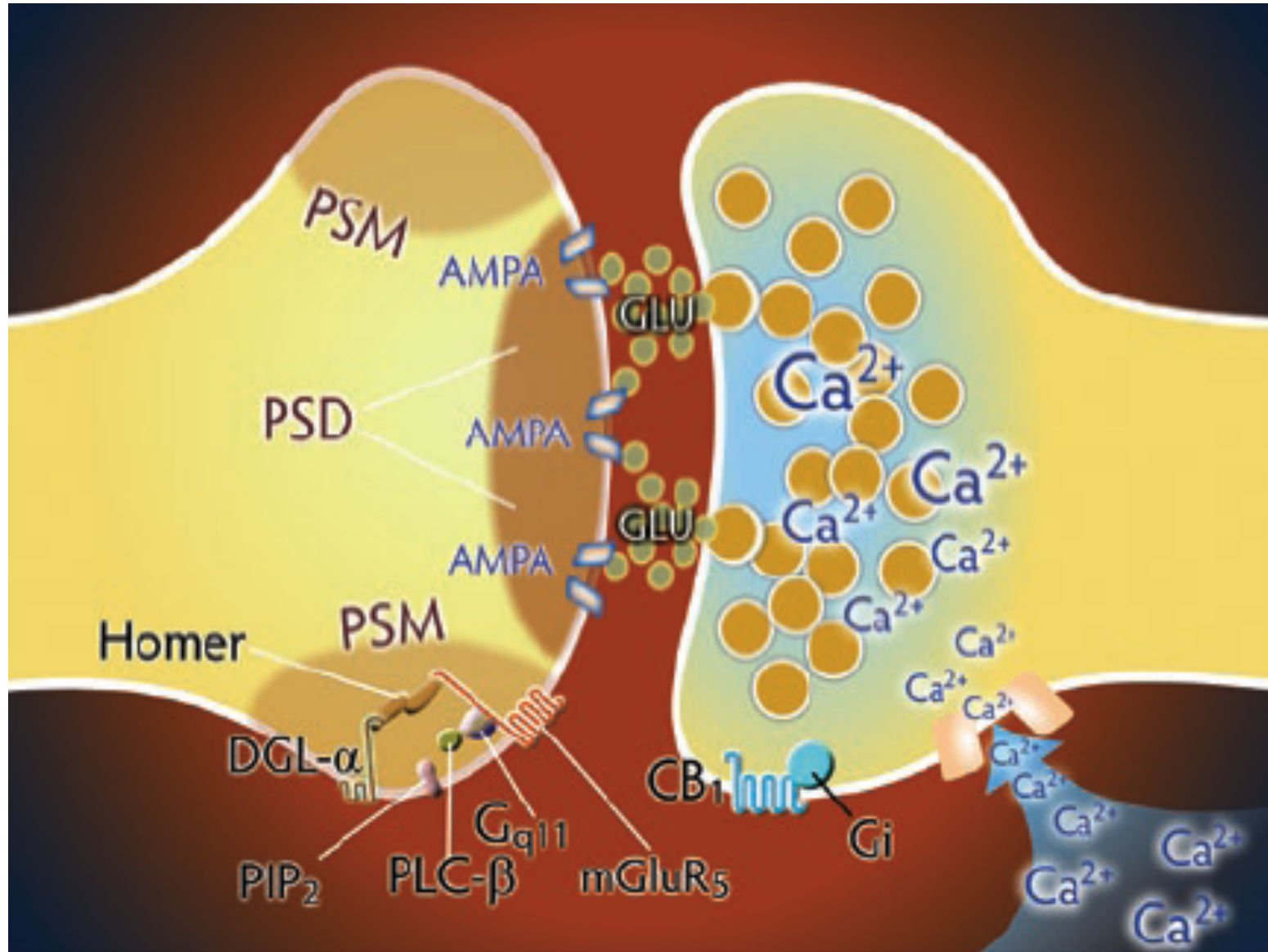
Synapses on dendrite & spine organization



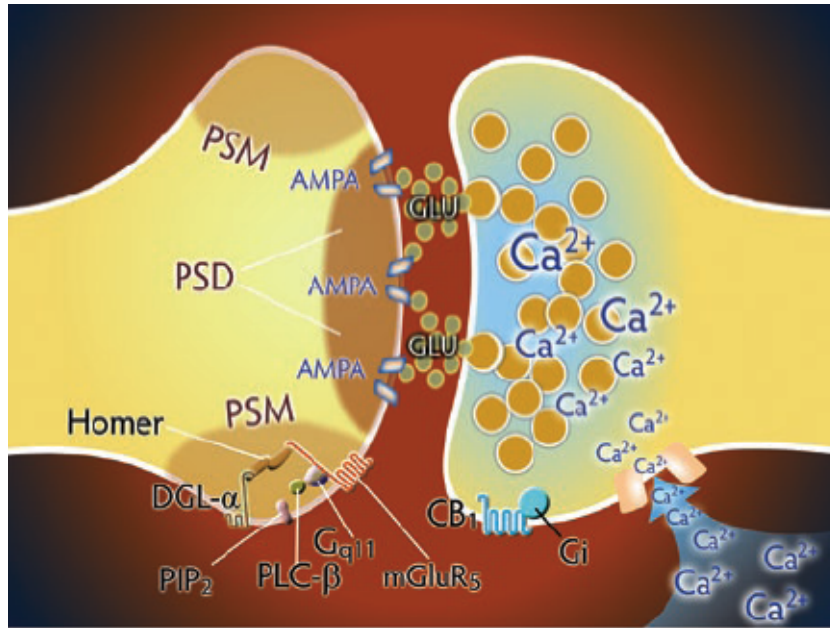
Образование 2-AG



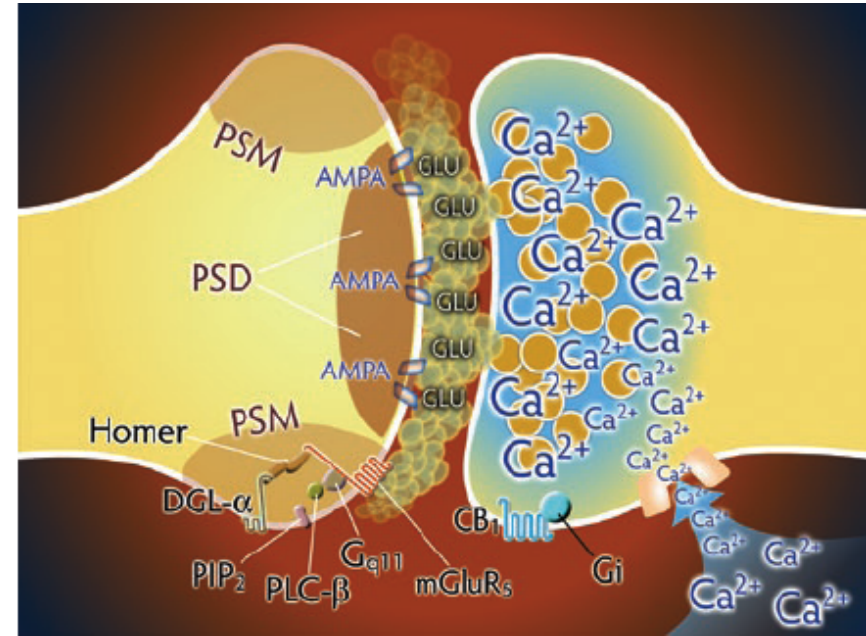
Retrograde EC action through Perisynaptic Signaling Machinery (PSM)



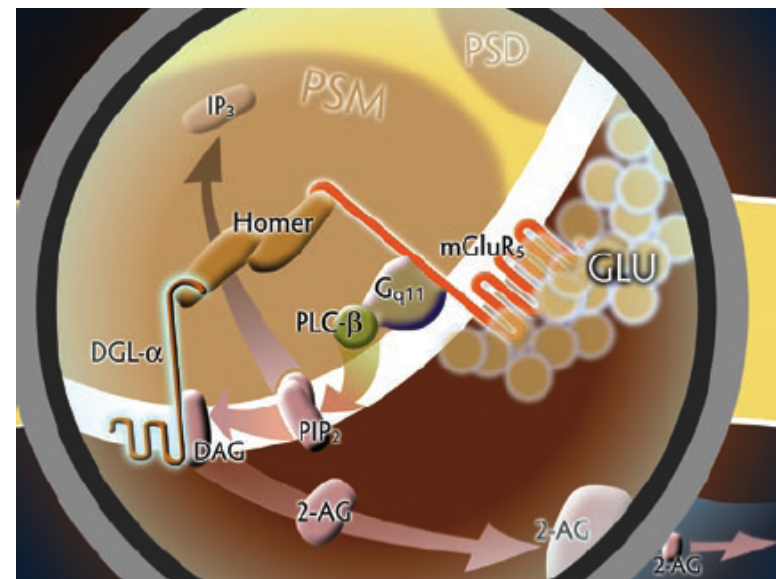
Low activity



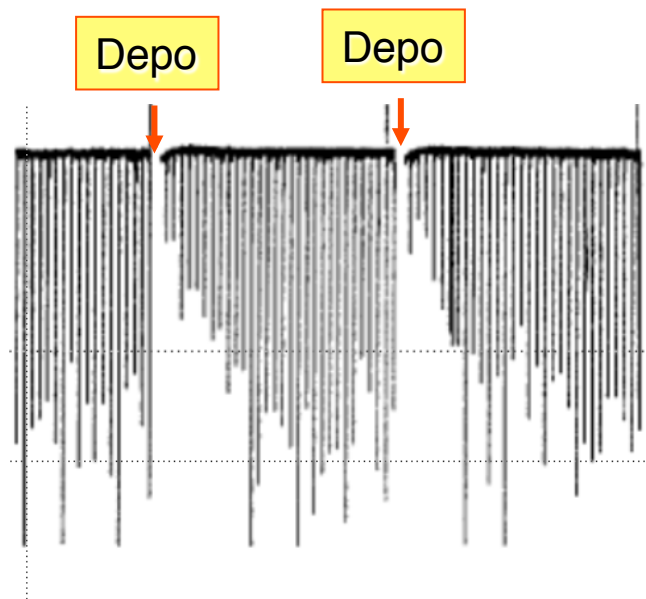
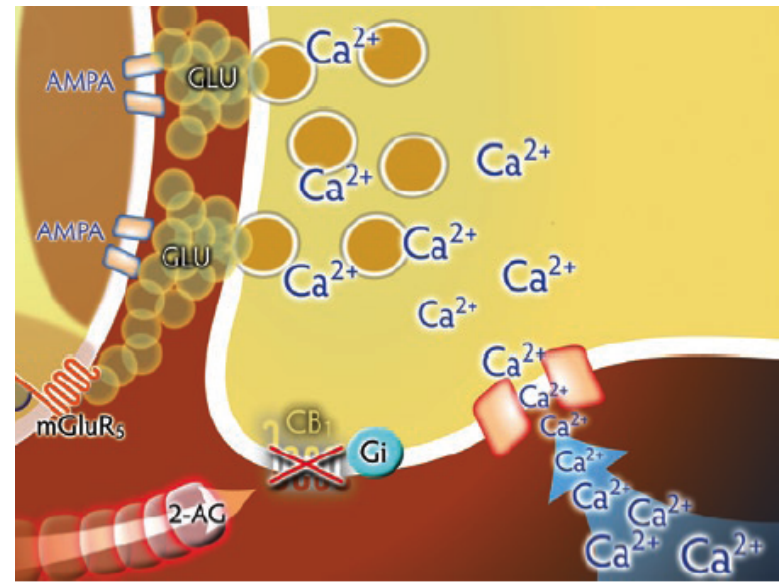
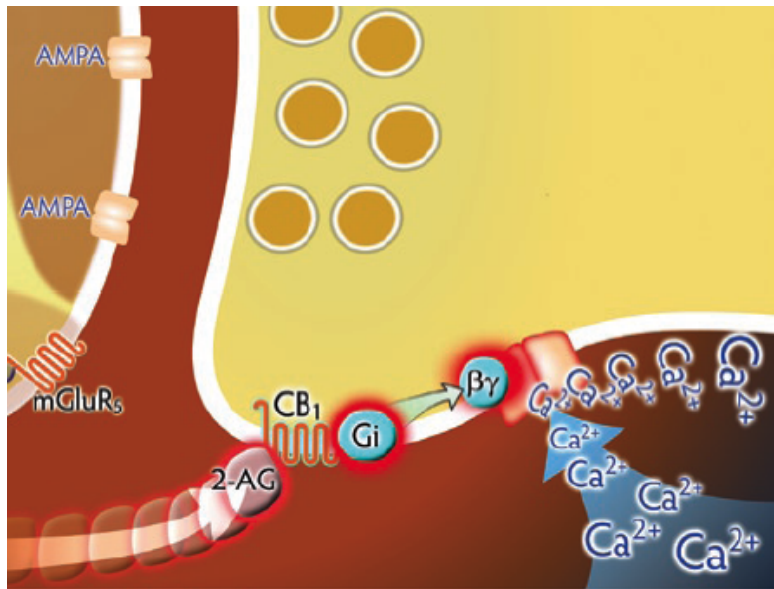
High activity



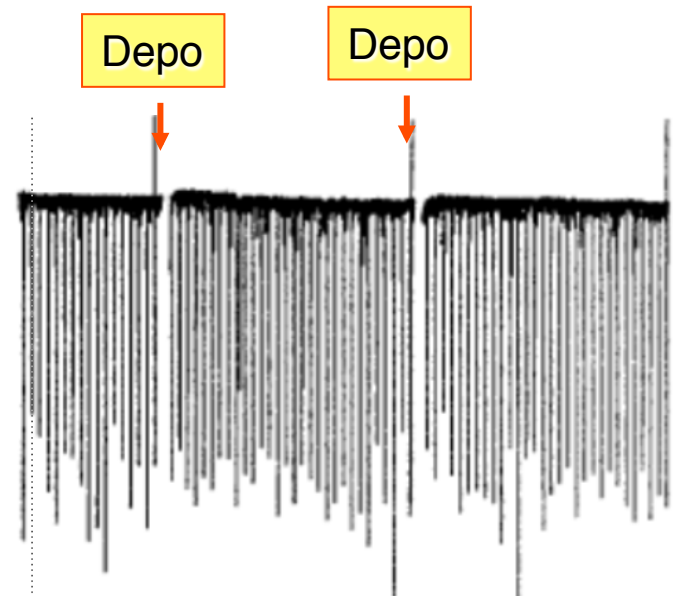
Activation of perisynaptic signaling machinery



Modulation of Ca Channels and NT release by 2-AG

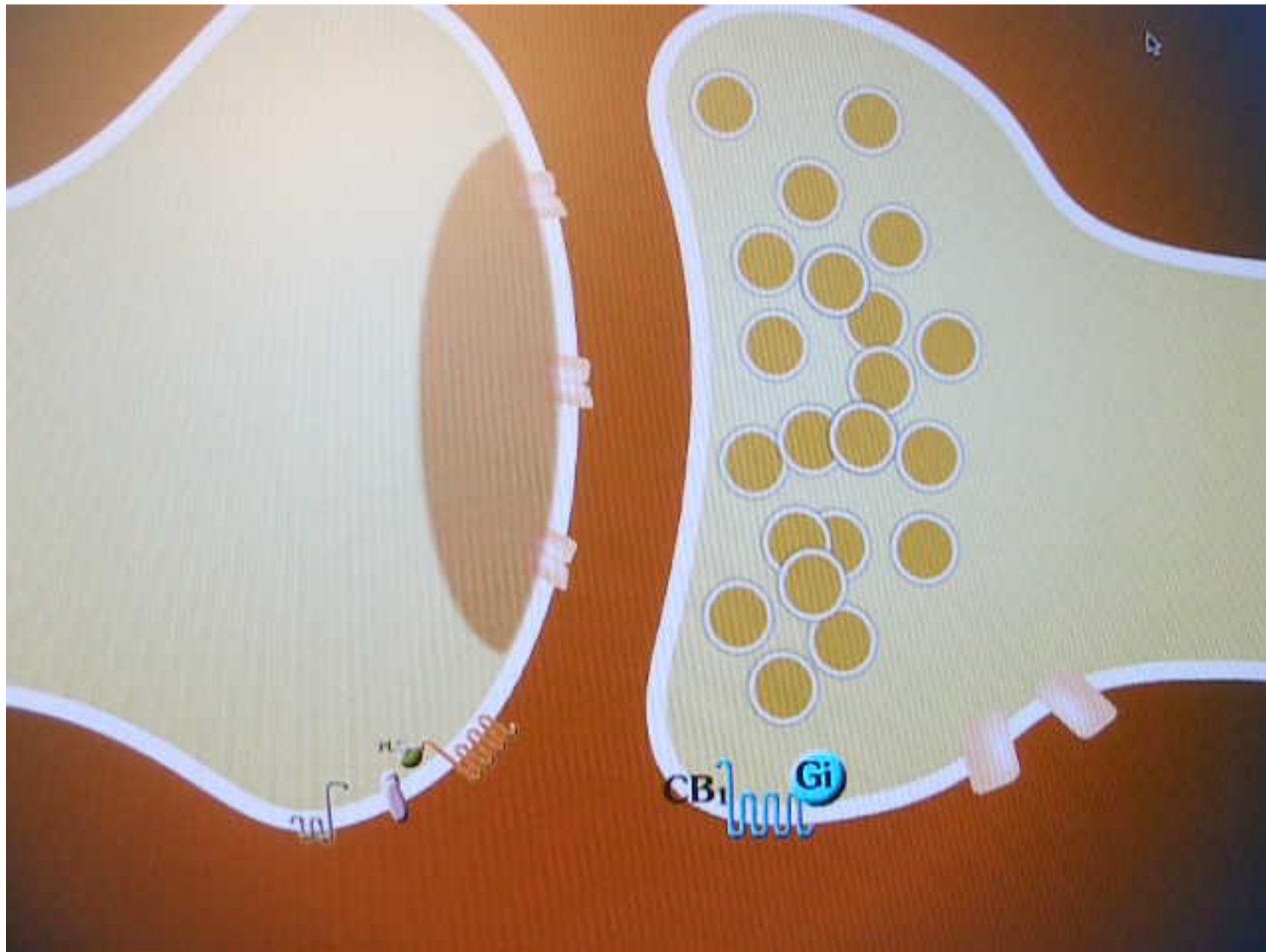


Control



CB1 R blocked

Suggested mechanism of 2-AG action in excitatory synapses



На память:

Эндоканнабиноиды в регуляции процессов физиологии и патологии

- Большинство CB1 рецепторов находятся на пресинаптических терминалях аксонов. Активация CB1 рецепторов приводит к торможению выброса нейромедиатора.
- Эндоканнабиноиды:
 - подавление поведенческих реакций на вредные воздействия
 - ослабление ноцицептивных сигналов через активацию CB1 и CB2 рецепторов
 - Регулирование приема пищи
 - Иммуномодуляция
 - Воспаление
 - Рак
 - Эпилепсия

Последствия систематического курения марихуаны и её подвидов:

- нарушение координации движений
- увеличение времени реакции
- снижение подвижности глазных яблок
- падение остроты зрения и нарушение цветовосприятия
- возможна дегенерация сетчатки и зрительных нервов
- сексуальная "некомпетентность"
- стенокардия и аритмия сердца.

Suggested reading

Alger BE. Retrograde signaling in the regulation of synaptic transmission: focus on endocannabinoids. *Prog Neurobiol*. 2002 Nov;68(4):247-86.

Chevaleyre V, Takahashi KA, Castillo PE. Endocannabinoid-mediated synaptic plasticity in the CNS. *Annu Rev Neurosci*. 2006;29:37-76

Diana MA, Bregestovski P. Calcium and endocannabinoids in the modulation of inhibitory synaptic transmission. *Cell Calcium*. 2005 May;37(5):497-505.

Howlett AC, Breivogel CS, Childers SR, Deadwyler SA, Hampson RE, Porrino LJ. Cannabinoid physiology and pharmacology: 30 years of progress. *Neuropharmacology*. 2004;47 Suppl 1:345-58.

Kano M, Ohno-Shosaku T, Hashimotodani Y, Uchigashima M, Watanabe M. Endocannabinoid-mediated control of synaptic transmission. *Physiol Rev*. 2009 Jan;89(1):309-80.

Onaivi ES. Cannabinoid receptors in brain: pharmacogenetics, neuropharmacology, neurotoxicology, and potential therapeutic applications. *Int Rev Neurobiol*. 2009;88:335-69.

